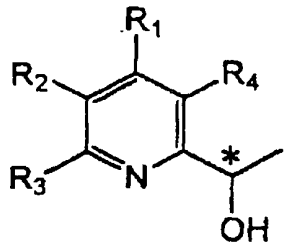
CLAIMS

1. A method of producing an optically active pyridineethanol derivative represented by the general formula [2]:



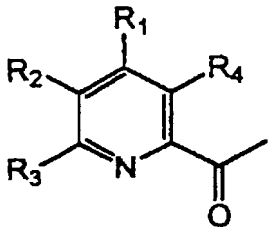
[2]

wherein R_1 and R_2 are bound to each other to form a 5- to 8-membered monocyclic heterocycle containing at least one hetero atom selected from the group consisting of oxygen, sulfur and nitrogen atoms, which heterocycle may optionally have a substituent(s), or a polycyclic heterocycle resulting from the condensation of such monocyclic heterocycle with another ring, which polycyclic heterocycle may optionally have a substituent(s),

R_3 and R_4 are the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group containing 1 to 12 carbon atoms, which may optionally have a substituent(s), or an alkoxy group containing 1 to 12 carbon atoms, which may optionally have a substituent(s),

and * indicates that the asterisked carbon atom is an asymmetric one,

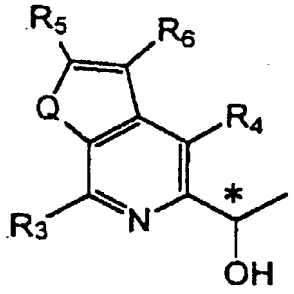
which method comprises stereoselectively reducing an acetylpyridine derivative represented by the general formula [1]:



[1]

wherein R_1, R_2, R_3 and R_4 are as defined above,
by causing an enzyme or enzyme source capable of asymmetrically reducing the same to act thereon.

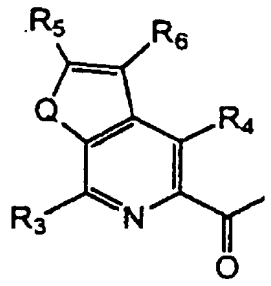
2. A method of producing an optically active pyridineethanol derivative represented by the general formula [4]:



[4]

wherein Q represents an oxygen or sulfur atom or a group of the general formula -N(D)-, in which N is a nitrogen atom and D represents a hydrogen atom or a monovalent protective group, R_3, R_4, R_5 and R_6 are the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group containing 1 to 12 carbon atoms, which may optionally have a substituent(s), or an alkoxy group containing 1 to 12 carbon atoms, which may optionally have a substituent(s),
and * indicates that the asterisked carbon atom is an asymmetric one,

which method comprises stereoselectively reducing an acetylpyridine derivative represented by the general formula [3]:



[3]

wherein Q, R_3, R_4, R_5 and R_6 are as defined above, by causing an enzyme or enzyme source capable of asymmetrically reducing the same to act thereon.

3. The production method according to Claim 2, wherein Q is an oxygen atom.

4. The production method according to Claim 2, wherein Q is an oxygen atom, R_3 is a hydrogen atom or a chlorine atom, R_4 is a hydrogen atom, R_5 is a hydrogen atom and R_6 is a hydrogen atom or a methyl group.

5. The production method according to Claim 2, wherein Q is an oxygen atom and R_3, R_4, R_5 and R_6 each is a hydrogen atom.

6. The production method according to any of Claims 1 to 5,

wherein the reaction is carried out in the presence of an enzyme capable of reducing the oxidized form nicotinamide adenine dinucleotide and/or the oxidized form nicotinamide adenine dinucleotide phosphate to the respective reduced forms as well as a substrate for the reduction.

7. The production method according to Claim 6, wherein said enzyme for reduction to the reduced form is

glucose dehydrogenase
and said substrate for reduction is glucose.

8. The production method according to Claim 6, wherein said enzyme for reduction to the reduced form is formate dehydrogenase
and said substrate for reduction is formic acid.

9. The production method according to any of Claims 1 to 8,
wherein said enzyme or enzyme source is derived from a microorganism selected from the group consisting of microorganisms of the genera Ashbya, Candida, Cryptococcus, Clavispora, Debaryomyces, Dipodascus, Galactomyces, Geotrichum, Guilliermondella, Hanseniaspora, Hansenula, Hyphopichia, Issatchenkia, Kluyveromyces, Kuraishia, Lodderomyces, Metschnikowia, Ogataea, Pachysolen, Pichia, Rhodosporidium, Rhodotorula, Saccharomycopsis, Schwanniomyces, Sporidiobolus, Sporobolomyces, Schizoblastosporion, Stephanoascus, Torulaspora, Trigonopsis, Trichosporon, Willopsis, Yamadazyma, Zygosaccharomyces, Alcaligenes, Bacillus, Brevibacterium, Cellulomonas, Corynebacterium, Jensenia, Ochrobactrum, Pseudomonas, Rhodococcus and Tsukamurella.

10. The production method according to Claim 9,
wherein the product optically active pyridineethanol derivative has the S absolute configuration
and said enzyme or enzyme source is derived from a microorganism selected from the group consisting of microorganisms of the genera Ashbya, Candida, Cryptococcus, Clavispora, Debaryomyces, Dipodascus, Galactomyces, Geotrichum, Guilliermondella, Hanseniaspora, Hansenula, Hyphopichia, Issatchenkia, Kluyveromyces, Kuraishia, Lodderomyces, Metschnikowia, Ogataea, Pachysolen, Pichia,

Rhodosporidium, Rhodotorula, Saccharomycopsis, Schwanniomyces, Sporidiobolus, Sporobolomyces, Schizoblastosporion, Stephanoascus, Torulaspora, Trigonopsis, Trichosporon, Willopsis, Yamadazyma, Zygosaccharomyces, Alcaligenes, Bacillus, Brevibacterium, Cellulomonas, Corynebacterium, Jensenia, Ochrobactrum, Pseudomonas, Rhodococcus and Tsukamurella.

11. The production method according to Claim 9, wherein the product optically active pyridineethanol derivative has the R absolute configuration and said enzyme or enzyme source is derived from a microorganism selected from the group consisting of microorganisms of the genera Candida, Ogataea, Pichia, Yamadazyma, Brevibacterium and Corynebacterium.

12. An enzyme having the following physical and chemical properties (1) to (3):

(1) Activity: It stereoselectively reduces 5-acetylfuro[2,3-c]pyridine, in the presence of reduced form nicotinamide adenine dinucleotide as a coenzyme, to give 5-(1-(R)-hydroxyethyl)furo[2,3-c]pyridine;

(2) Specificity: It has reducing ability against ketones and aldehydes but is very low in reducing activity against carbocyclic ketones and the α-position keto group of α-keto acids;

(3) Molecular weight: It shows a molecular weight of about 60,000 in gel filtration analysis and a molecular weight of about 29,000 in SDS polyacrylamide electrophoresis.

13. The enzyme according to Claim 12 which has the following physical and chemical properties (4) to (6):

(4) Optimal temperature: 50 ℃ to 55 ℃;

(5) Optimal pH: 5.0 to 6.0;

(6) Inhibitor: It is inhibited by the mercury ion.

14. An enzyme specified below under (a) or (b):
(a) An enzyme comprising an amino acid sequence shown under SEQ ID NO:1 in the sequence listing;
(b) An enzyme comprising an amino acid sequence derived from the amino acid sequence shown under SEQ ID NO:1 in the sequence listing by deletion, substitution and/or addition of one or several amino acids and having an activity by which 5-acetylfuro[2,3-c]pyridine is stereoselectively reduced to 5-(1-(R)-hydroxyethyl)furo[2,3-c]pyridine.

15. The enzyme according to any of Claims 12 to 14 which is derived from a microorganism belonging to the genus Candida.

16. The enzyme according to any of Claims 12 to 14 which is derived from Candida maris.

17. The enzyme according to any of Claims 12 to 14 which is derived from Candida maris IFO 10003.

18. The production method according to any of Claims 1 to 8,
wherein said enzyme is defined according to any of Claims 12 to 17
and the product optically active pyridineethanol derivative has the R absolute configuration.

19. A DNA coding for the enzyme according to any of Claims 14 to 17.

20. A DNA comprising a base sequence shown under SEQ ID NO:2 in the sequence listing.

21. A recombinant vector containing the DNA according to Claim 19 or 20.

22. The recombinant vector according to Claim 21 which is pNTFP.

23. The recombinant vector according to Claim 21 which comprises a DNA coding for glucose dehydrogenase.

24. The recombinant vector according to Claim 23, wherein said glucose dehydrogenase is derived from Bacillus megaterium.

25. The recombinant vector according to Claim 24 which is pNTFPG.

26. A transformant having the recombinant vector according to any of Claims 21 to 25.

27. The transformant according to Claim 26, wherein the host is Escherichia coli.

28. The transformant according to Claim 27 which is Escherichia coli HB101 (pNTFP).

29. The transformant according to Claim 27 which is Escherichia coli HB101 (pNTFPG).

30. A transformant having a first recombinant vector containing the DNA according to Claim 19 or 20 and a second recombinant vector containing a DNA coding for glucose dehydrogenase.

31. The transformant according to Claim 30, wherein said first recombinant vector is pNTFP

and said glucose dehydrogenase is derived from Bacillus megaterium.

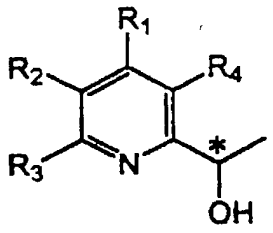
32. The transformant according to Claim 30 or 31, wherein the host is Escherichia coli.

33. The production method according to any of Claims 1 to 5,

wherein said enzyme is the transformant according to any of Claims 26 to 32

and said product optically active pyridineethanol derivative has the R absolute configuration.

34. A method of producing an optically active pyridineethanol derivative having the S absolute configuration and represented by the general formula [6]:



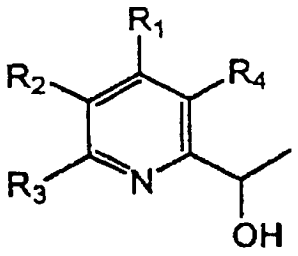
[6]

wherein R_1 and R_2 are bound to each other to form a 5- to 8-membered monocyclic heterocycle containing at least one hetero atom selected from the group consisting of oxygen, sulfur and nitrogen atoms, which heterocycle may optionally have a substituent(s), or a polycyclic heterocycle resulting from the condensation of such monocyclic heterocycle with another ring, which polycyclic heterocycle may optionally have a substituent(s),

and R_3 and R_4 are the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group containing 1 to 12 carbon atoms, which may optionally have a substituent(s), or an alkoxy group containing 1 to 12 carbon

atoms, which may optionally have a substituent(s), and * indicates that the asterisked carbon atom is an asymmetric one,

which method comprises causing the enzyme according to any of Claims 12 to 17 and/or the transformant according to any of Claims 26 to 32 to act on a pyridineethanol derivative represented by the general formula [5]:

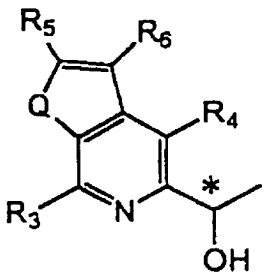


[5]

wherein R_1, R_2, R_3 and R_4 are as defined above, to thereby preferentially oxidize the R form of the pyridineethanol derivative

and recovering the remaining S form of the pyridineethanol derivative.

35. A method of producing an optically active pyridineethanol derivative having the S absolute configuration and represented by the general formula [8]:



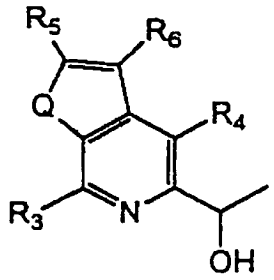
[8]

wherein Q represents an oxygen or sulfur atom or a group of the general formula -N(D)-, in which N is a nitrogen atom and D represents a hydrogen atom or a monovalent protective group, R_3, R_4, R_5 and R_6 are the same or different and each represents

a hydrogen atom, a halogen atom, a hydroxyl group, an alkyl group containing 1 to 12 carbon atoms, which may optionally have a substituent(s), or an alkoxy group containing 1 to 12 carbon atoms, which may optionally have a substituent(s),

and * indicates that the asterisked carbon atom is an asymmetric one,

which method comprises causing the enzyme according to any of Claims 12 to 17 and/or the transformant according to any of Claims 26 to 32 to act on a pyridineethanol derivative represented by the general formula [7]:



[7]

wherein Q, R_3, R_4, R_5 and R_6 are as defined above,

to thereby preferentially oxidize the R form of the pyridineethanol derivative

and recovering the remaining S form of the pyridineethanol derivative.

36. The production method according to Claim 35, wherein Q is an oxygen atom.

37. The production method according to Claim 35, wherein Q is an oxygen atom,
R_3 is a hydrogen atom or a chlorine atom,
R_4 is a hydrogen atom,
R_5 is a hydrogen atom
and R_6 is a hydrogen atom.